Attorney Docket No.: AVZ-007CP3 Group Art Unit: 1625

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

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Listing of Claims:

Claims 1-85 (Canceled).

86. [Currently Amended] A method for treating Parkinson's disease in a subject, comprising:

administering to a subject a therapeutically effective amount of a combination of creatine, a creatine phosphate or a creatine compound and a neuroprotective agent, such that Parkinson's disease in said subject is treated, wherein said neuroprotective agent is selected from the group consisting of inhibitors of glutamate excitotoxicity, 2,3 dimethoxy-5-methyl-6-decaprenyl benoquinone, nicotinamide, spin traps, growth factors, nitric oxide synthase inhibitors, cyclooxygenase 2 inhibitors, aspirin, ICE inhibitors, neuroimmunophilis, N-acetylcysteine, antioxidants, lipoic acid, cofactors, riboflavin, and CoQ10, wherein said creatine compound has the formula:

$$Z_1$$
 $C = X - A - Y$
 Z_2

and pharmaceutically acceptable salts thereof, wherein:

- a) Y is selected from the group consisting of: -CO₂H, -NHOH, -NO₂, -SO₃H, -C(-0)NHSO₂J and -P(-O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C₁-C₆ straight chain alkyl, C₂-C₆ branched alkyl, C₂-C₆ alkenyl, C₂-C₆ branched alkenyl, and aryl;
- b) A is selected from the group consisting of: C, CH, C₁-C₅alkyl, C₂-C₅alkenyl, C₂-C₅alkynyl, and C₁-C₅ alkoyl chain, each having 0-2 substituents which are selected independently from the group consisting of:
- 1) K, where K is selected from the group consisting of: C_1 - C_6 straight alkyl, C_2 - C_6 straight alkenyl, C_1 - C_6 straight alkoyl, C_3 - C_6 branched alkyl,

U.S.S.N. 09/687,575 Examiner: R. Covington Attorney Docket No.: AVZ-007CP3 Group Art Unit: 1625 C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; 2) an aryl-group, wherein the aryl-group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH2L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; and -NH-M, wherein M is selected from the group consisting of: 23) hydrogen, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₁-C₄ alkoyl, C₃-C₄ branched alkyl, C₃-C₄ branched alkenyl, and C₄ branched alkoyl; c) X is selected from the group consisting of NR₁, CHR₁, CR₁, O and S, wherein R₁ is selected from the group consisting of: hydrogen; 1) K where K is selected from the group consisting of: C₁-C₆ straight 2) alkyl, C2-C6 straight alkenyl, C1-C6 straight alkoyl, C3-C6 branched alkyl, C3-C6 branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; 3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0 2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

d) Z_1 and Z_2 are chosen independently from the group consisting of: =0, -NHR₂, -CH₂R₂, -NR₂OH; wherein Z_1 and Z_2 may not both be =0 and wherein R₂ is selected from the group consisting of:

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- 1) hydrogen;
- 2) K, where K is selected from the group consisting of: C₁-C₆ straight alkyl; C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, ehloro, epoxy and acetoxy;
 - <u>34</u>) a C₄-C₈ a-amino-carboxylic acid attached via the w-carbon; <u>and</u>
- B, wherein B is selected from the group consisting of: -CO₂H, -NHOH, -SO₃H, and -NO₂, $\frac{OP(-O)(OH)(OJ)}{OH(OJ)}$ and -P(-O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C₁-C₆ straight alkyl, C₃-C₆ branched alkyl, C₂-C₆ alkenyl, C₃-C₆ branched alkenyl, and aryl, wherein B is optionally connected to the nitrogen via a linker selected from the group consisting of: C₁-C₂ alkyl, C₂ alkenyl, and C₁-C₂ alkoyl_{\pm};
- 6) D-E, wherein D is selected from the group consisting of: C₁-C₃ straight alkyl, C₃ branched alkyl, C₂-C₃ straight alkenyl, C₃ branched alkenyl, C₁-C₃ straight alkoyl, aryl and aroyl; and E is selected from the group consisting of: (PO₃)_nNMP, where n is 0-2 and NMP is ribonucleotide monophosphate connected via the 5' phosphate, 3' phosphate or the aromatic ring of the base; [P(=O)(OCH₃)(0)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; [P(=O)(OH)(CH₂)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, OG, C(=O)G, and CO₂G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ branched

alkyl, C₃-C₆-branched alkenyl, C₄-C₆-branched alkoyl, wherein E may be attached to any point to D, and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and

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7)—E, wherein E is selected from the group consisting of (P0₃)_nNMP, where n is 0 2 and NMP is a ribonucleotide monophosphate connected via the 5' phosphate, 3' phosphate or the aromatic ring of the base; [P(=O)(OCH₃)(0)]_m·Q, where m is 0 3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; [P(=O)(OH)(CH₂)]_m·Q, where m is 0 3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0 3 substituents chose independently from the group consisting of: C₁, Br, epoxy, acetoxy, OG, C(=O)G, and CO=G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl; and if E is aryl, E may be connected by an amide linkage;

е)	if R ₄ and at least	one R ₂ group	are present, F	५ may be conn	ected by a
single or doub	ole bond to an R2-	group to form	a cycle of 5 to	o 7 members;	

- f) if two R₂ groups are present, they may be connected by a single or a double bond to form a cycle of 4 to 7 members; and
- g)—if R_1 is present and Z_1 or Z_2 is selected from the group consisting of NHR₂, CH₂R₂ and NR₂OH, then R_1 may be connected by a single or double bond to the carbon or nitrogen of either Z_1 or Z_2 to form a cycle of 4 to 7 members.

Claims 87-90 (Cancelled).

- 91. [Currently Amended] The method of claim 86 or 133, wherein said neuroprotective agent is a spin trap.
- 92. [Previously Presented] The method of claim 91, wherein said spin trap is PBN.
- 93. [Currently Amended] The method of claim 86 or 133, wherein said neuroprotective agent is a cofactor for normal cellular metabolism.

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94. [Previously Presented] The method of claim 93, wherein said cofactor is carnitine.

- 95. [Currently Amended] The method of claim 86 or 133, wherein said neuroprotective agent is an antioxidant.
- 96. [Previously Presented] The method of claim 95, wherein said antioxidant is vitamin E.
- 97. [Cancelled]
- 98. [Currently Amended] The method of claim 86 or 133, wherein said neuroprotective agent is riboflavin.
- 99. [Currently Amended] The method of claim 86 or 133, further comprising administering at least one additional neuroprotective agent or creatine compound.
- 100. [Currently Amended] The method of claim 86 or 133, wherein said creatine compound is creatine.

Claims 101-107 (Canceled).

108. [Currently Amended] A method for treating Huntington's disease in a subject, comprising:

administering to a subject a therapeutically effective amount of a combination of creatine, a creatine phosphate or a creatine compound and a neuroprotective agent, such that Huntington's disease is treated, wherein said neuroprotective agent is selected from the group consisting of inhibitors of glutamate excitotoxicity, 2,3 dimethoxy-5-methyl-6-decaprenyl benoquinone, nicotinamide, spin traps, growth factors, nitric oxide synthase inhibitors, cyclooxygenase 2 inhibitors, aspirin, ICE inhibitors, neuroimmunophilis, N-acetylcysteine, antioxidants, lipoic acid, cofactors, riboflavin, and CoQ10, wherein said creatine compound has the formula:

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$$Z_1$$
 $C = X - A - Y$

and pharmaceutically acceptable salts thereof, wherein:

- Y is selected from the group consisting of: -CO₂H, -NHOH, -NO₂, -SO₂H, C(-0)NHSO₂J and P(-O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C1 C6 straight chain alkyl, C2 C6 branched alkyl, C2 C6 alkenyl, C₃-C₆-branched alkenyl, and aryl;
- A is selected from the group consisting of: C, CH, C₁-C₅alkyl, C₂-C5alkenyl, C2-C5alkynyl, and C1-C5 alkoyl chain, each having 0-2 substituents which are selected independently from the group consisting of:
- K, where K is selected from the group consisting of: C_1 - C_6 1) straight alkyl, C2-C6 straight alkenyl, C1-C6 straight alkoyl, C3-C6 branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- 2) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH2L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; and
- -NH-M, wherein M is selected from the group consisting of: hydrogen, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₁-C₄ alkoyl, C₃-C₄ branched alkyl, C₃-C₄ branched alkenyl, and C4 branched alkoyl;
- X is selected from the group consisting of NR₁, CHR₁, CR₁, O and S, wherein R_1 is selected from the group consisting of:
 - 1) hydrogen;
- K where K is selected from the group consisting of: C₁-C₆ straight 2) alkyl, C2-C6 straight alkenyl, C1-C6 straight alkoyl, C3-C6 branched alkyl, C3-C6

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branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: CH₂L and COCH₂L where L is independently selected from the group consisting of: bromo,

- 4) a C₅ C₉ a amino w methyl w adenosylcarboxylic acid attached via the w methyl carbon;
- _____5) __a C₅-C₉ a amino w aza w methyl w adenosylcarboxylic acid attached via the w methyl carbon; and
- 6) a C₅-C₉ a amino w thia w methyl w adenosylcarboxylic acid attached via the w methyl carbon;
- d) Z_1 and Z_2 are chosen independently from the group consisting of: =0, -NHR₂, -CH₂R₂, -NR₂OH; wherein Z_1 -and Z_2 -may not both be =0 and wherein R₂ is selected from the group consisting of:
 - 1) hydrogen;

chloro, epoxy and acetoxy;

- 2) K, where K is selected from the group consisting of: C₁-C₆ straight alkyl; C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
 - <u>34</u>) a C₄-C₈ a-amino-carboxylic acid attached via the w-carbon; <u>and</u>

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B, wherein B is selected from the group consisting of: $-CO_2H$, -NHOH, $-SO_3H$, and $-NO_2$, OP(-O)(OH)(OJ) and -P(-O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C_1 - C_6 straight alkyl, C_3 - C_6 branched alkyl, C_2 - C_6 alkenyl, C_3 - C_6 branched alkenyl, and aryl, wherein B is optionally connected to the nitrogen via a linker selected from the group consisting of: C_1 - C_2 alkyl, C_2 alkenyl, and C_1 - C_2 alkoyl.

6) — D E, wherein D is selected from the group consisting of: C₁-C₃ straight alkyl, C₃-branched alkyl, C₂-C₃-straight alkenyl, C₃-branched alkenyl, C₁-C₃ straight alkoyl, aryl and aroyl; and E is selected from the group consisting of: -(P0₃)_nNMP, where n is 0 2 and NMP is ribonucleotide monophosphate connected via the 5' phosphate, 3' phosphate or the aromatic ring of the base; [P(-O)(OCH₃)(0)]_m-Q, where m is 0 3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; [P(-O)(OH)(CH₂)]_m-Q, where m is 0 3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0 3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, -OG, -C(-O)G, and -CO₂G, where G is independently selected from the group consisting of: C₁-C₆-straight alkyl, C₂-C₆-branched alkenyl, C₁-C₆-branched alkenyl, C₃-C₆-branched alkenyl, C₄-C₆-branched alkenyl, wherein E may be attached to any point to D, and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and

(P0₃)_nNMP, where n is 0 2 and NMP is a ribonucleotide monophosphate connected via the 5' phosphate, 3' phosphate or the aromatic ring of the base; [P(=O)(OCH₃)(0)]_m Q, where m is 0 3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; [P(=O)(OH)(CH₂)]_m Q, where m is 0 3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0 3 substituents chose independently from the group consisting of: C₁, Br, epoxy, acetoxy, OG, C(=O)G, and CO=G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl; and if E is aryl, E may be connected by an amide linkage;

e) if R₁ and at least one R₂ group are present, R₁ may be connected by a single or double bond to an R₂ group to form a cycle of 5 to 7 members;

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f) if two R₂ groups are present, they may be connected by a single or a double bond to form a cycle of 4 to 7 members; and

g) if R_1 is present and Z_1 or Z_2 is selected from the group consisting of NHR2, CH2R2 and NR2OH, then R_1 may be connected by a single or double bond to the carbon or nitrogen of either Z_1 or Z_2 to form a cycle of 4 to 7 members.

Claims 109-112 (Cancelled).

- 113. [Currently Amended] The method of claim 108 or 134, wherein said neuroprotective agent is a spin trap.
- 114. [Previously Presented] The method of claim 113, wherein said spin trap is PBN.
- 115. [Currently Amended] The method of claim 108 or 134, wherein said cofactor is a cofactor for normal cellular metabolism.
- 116. [Previously Presented] The method of claim 115, wherein said cofactor is carnitine.
- 117. [Currently Amended] The method of claim 108 or 134, wherein said neuroprotective agent is an antioxidant.
- 118. [Previously Presented] The method of claim 117, wherein said antioxidant is vitamin E.
- 119. [Cancelled].
- 120. [Previously Presented] The method of claim 117, wherein said neuroprotective agent is riboflavin.
- 121. [Currently Amended] The method of claim 108 or 134, further comprising administering at least one additional neuroprotective agent or creatine compound.

122. [Currently Amended] The method of claim 108 or 134, wherein said creatine compound is creatine.

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Claim 123-132 (Canceled).

pharmaceutically acceptable salts thereof.

134. [New] A method for treating Huntington's disease in a subject, comprising:

administering to a subject a therapeutically effective amount of a combination of creatine, a creatine phosphate or a creatine compound and a neuroprotective agent, such that Huntington's disease is treated, wherein said neuroprotective agent is selected from the group consisting of inhibitors of glutamate excitotoxicity, 2,3 dimethoxy-5-methyl-6-decaprenyl benoquinone, nicotinamide, spin traps, growth factors, nitric oxide synthase inhibitors, cyclooxygenase 2 inhibitors, aspirin, ICE inhibitors, neuroimmunophilis, N-acetylcysteine, antioxidants, lipoic acid, cofactors, riboflavin, and CoQ10, wherein said creatine compound is selected from the group consisting of:

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acceptable salts thereof.